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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/773,785

02/06/2004

Eric Finzi

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EXAMINER,

FORD, VANESSA L

ART UNIT

PAPER NUMBER

1645

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/23/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/773,785	Applicant(s) FINZI, ERIC	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed December 26, 2006. Claims 1-2, 6, 8, 14, 17 and 20 have been amended. Claim 22 has been added. Claims 1-22 are under examination.

Rejections Objection/Withdrawn

2. In view of Applicant's amendment and remarks the following rejections are withdrawn.

- a) Objection to the specification, paragraph 2, page 1.
- b) rejection of claims 1-7, 16-18 and 20-21 under 35 U.S.C.112, second paragraph, page 2, paragraph 2.
- c) rejection of claims 6, 7, 14 and 15 under 35 U.S.C. 112, second paragraph, page 3, paragraph 3.
- b) rejection of claims 1-7, 16-18 and 20-21 under 35 U.S.C.112, second paragraph, page 3, paragraph 4.
- b) rejection of claims 8-15 and 19 under 35 U.S.C.112, second paragraph, page 3, paragraph 5.

Rejections Maintained

3. The rejection of claims 1-15 and newly submitted claim 22 under 35

U.S.C. 103(a) is maintained for the reasons set forth on pages 4-7, paragraph 6 of the previous Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

It should be noted that the Examiner is interpreting "downturned mouth" or "sad mouth" as frowning, scowl or the appearance of the patient to be sad.

The rejection was on the grounds that the claims are directed to a method of treating depression in a subject comprising administering a therapeutically effective amount of a neurotoxin to a facial muscle to cause paralysis of the facial muscle, thereby affecting the ability of the subject to frown and treating depression in the subject.

Murry et al teach a method of treating depression in spasmodic dysphonia patients who suffered from depression and anxiety (see the Abstract). Murry et al teach that depression and anxiety levels were significantly reduced approximately 1 week after patients were injected with botulinum toxin (see the Abstract). Murry et al teach that spasmodic dystonia has been reported to be highly linked with emotional trauma (page 310).

Murry et al do not teach administering botulinum toxin to a facial muscle such as a frontalis muscle, an orbicularis oculi muscle, procerus muscle, a corrugator supercilli muscle or depressor anguli oris muscle.

Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). Binder teaches that botulinum toxin when administered to patients with headaches is effective in reducing pain and symptoms associated with or the onset of headaches in mammals (see the Abstract). Binder teaches that botulinum toxin can be administered in a dose of up to about 1,000 units although individual dosages of about 15-30 units are preferred (columns 5-6). Binder teaches that botulinum toxin injection can be effective up to about

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3 to 6 months (column 7). Therefore the combination of prior art references teach the claim limitation "...further comprising administering an additional dose of 30-50 unit equivalents of botulinum A to the facial muscle after about two to six months".

Murry et al and Binder do not teach the claim limitation "...affecting the ability of the subject to frown".

Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth (see the Abstract). Carruthers et al teach that this condition is called "sad mouth" (column 2).

It would be *prima facie* obvious at the time the invention was made to use botulinum toxin to treat patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Murry et al teach that administering botulinum toxin to spasmodic dysphonia patients experiencing depression significantly reduced the levels of depression and anxiety in these patients and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to patients suffering from depression would be effective way to treat depression in these patients.

Applicant's Arguments

A) Applicant urges that Murray et al do not teach, nor render obvious, the injection of a neurotoxin into facial muscles. Applicant urges that Murray et al do not suggest, nor render obvious that depression could be treated using a neurotoxin nor do Murray et al suggest or render obvious the treatment of intermittent depression and anxiety.

B) Applicant urges that Binder teaches the reduction of headache pain by injecting botulinum toxin. Binder teaches that the preferred sites for injection are the face, head and neck. Applicant urges that Binder disclose that the effect of botulinum toxin is not related to spasm.

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C) Applicant urges that Carruthers et al teach the cosmetic use of botulinum toxin to paralyze the depressor anguli oris muscle to alleviate downturn of a subject's mouth (see the Abstract). Applicant urges that Carruthers et al do not teach or suggest the use of botulinum toxin to treat any emotional disorder, let alone depression.

D) Applicant urges that a *prima facie* case of obviousness has not been established. Applicant urges that none of Murray et al, Binder or Carruthers et al teaches the selection of a subject having a primary emotional disorder. Applicant urges that one would not necessarily expect that the injection of botulinum toxin into a facial muscle would result in the alleviation of a major depression or alleviation of intermittent anxiety and depression.

E) Applicant refers to Exhibit A Finzi et al to point out unexpected results.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 26, 2006 have been fully considered but they are not persuasive.

A) It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to

the claimed invention. It is the Examiner's position that the combination of references teaches the claimed invention.

To address Applicant's arguments regarding Murray et al, Murray et al teach that botulinum toxin is used to treat patients that have depression and anxiety. Murray et al teach that the levels of depression and anxiety were significantly reduced approximately 1 week after injection of botulinum toxin (see the Abstract). Murray et al do not teach administering botulinum toxin to a facial muscle nor does Murray et al teach the claim limitation "...affecting the ability of the subject to frown". However, Binder et al teach that botulinum toxin can be administered to various muscles in the face. To address Applicant comments regarding Murray et al not teaching the treatment of intermittent depression and anxiety, as stated above, Murray et al teach that depression and anxiety were significantly reduced 1 week after botulinum toxin injection. Murray et al teach that by the end of two months the effects of botulinum toxin began to wear off and there was an increase in anxiety (page 315). However, Binder teaches that subsequent injection of botulinum toxin should be administered to patients in about 3 month intervals (column 7).

B) To address Applicant's arguments regarding Binder, Binder et al teach that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with emotional states such as depression and tension (column 1). To

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address Applicant comments regarding muscle spasm, there are no limitations in the claims regarding muscle spasms.

C) To address Applicant's arguments regarding Carruthers et al, Carruthers teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn mouth (see the Abstract).. To address Applicant's comment regarding Carruthers et al not teaching depression or anxiety, it should be remembered that Murray et al teach treatment of depression and anxiety and it is the combination of references (Murray et al, Binder and Carruthers et al) that teach and suggest the claimed methods.

D) In response to applicant's argument that no case of *prima facie* obviousness was established using the references (Murray et al, Binder and Carruthers et al), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case,

One of ordinary skill would be motivated to use botulinum toxin to treat patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Murray et al teach that administering botulinum toxin to spasmodic dysphonia

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patients experiencing depression significantly reduced the levels of depression and anxiety in these patients and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth.

To address Applicant's comments regarding the expectation of the artisan of ordinary skill, it is the Examiner's position that the combination of references render the claimed invention obvious and based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to patients suffering from depression would be an effective way to treat depression in these patients. Further, the claims are not directed to a subject having a primary emotional disorder. It is noted that the Office is not suggesting that this limitation be added to the claims to overcome the prior art rejection.

E) To address Exhibit A, Finzi et al, while it is true that Finzi et al has established that botulinum toxin treats major depression, there is nothing on the record that suggests that the combination of references does not teach the claimed invention.

Claim 22 is directed to the method of claim 1, wherein the subject has major depression. Murray et al teach that 5 subjects used in the study were "highly" depressed patients. Murray et al teach that 4 of the 5 patients were considered clinically depressed with Self-rating of Depression Scale (SDS) scores ranging from 50

to 53 (page 313). Murray et al teach that patients with scores of 50 or above are in need of psychiatric care (page 313).

In view of all of the above, this rejection is maintained.

4. The rejection under 35 U.S.C. 103(a) is maintained for claims 1-7, 16-18 and newly submitted claim 22 for the reasons set forth on pages 6-8, paragraph 7 of the previous Office Action.

The rejection is reiterated below:

The rejection was on the grounds that the claims are directed to a method of treating depression in subject comprising administering a therapeutically effective amount of a neurotoxin to a facial muscle to cause paralysis of the facial muscle, thereby affecting the ability of the subject to frown and treating depression in the subject.

Jahanshahi et al teach that administration of botulinum toxin to patients with torticollis who also suffer from depression. Jahanshahi et al teach that botulinum toxin reduced depression but there was no significant improvement in body concept and self-esteem (see the Abstract). Jahanshahi et al suggest that use of other concepts or techniques may help with direct management of psychological aspects, body concept and low self-esteem (page 231).

Jahanshahi et al do not teach administering botulinum toxin to a facial muscle such as a frontalis muscle, an orbicularis oculi muscle, procerus muscle, a corrugator supercilli muscle or depressor anguli oris muscle.

Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). Binder teaches that botulinum toxin when administered to patients with headaches is effective in reducing pain and symptoms associated with or the onset of headaches in mammals (see the Abstract). Binder teaches that botulinum toxin can be administered in a dose of up to about 1,000 units although individual dosages of about 15-30 units are preferred (columns 5-6). Binder teaches that botulinum toxin injection be effective up to about 3 to 6 months (column 7). Therefore the combination of prior art references teach the claim limitation "...further comprising administering an additional dose of 30-50 unit equivalents of botulinum A to the facial muscle after about two to six months".

Jahanshahi et al and Binder do not teach claim limitation "... affecting the ability of the subject to frown".

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Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth (see the Abstract). Carruthers et al teach that this condition is called "sad mouth" column 2).

It would be *prima facie* obvious at the time the invention was made to administer botulinum toxin to patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Jahanshahi et al teach that administering botulinum toxin to torticollis patients experiencing depression significantly reduced levels of depression and anxiety, Binder teaches that botulinum toxin can be effectively administered to facial muscles such as the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to the facial muscles of patients suffering from depression would be an effective way to treat depression as well as anxiety in these patients.

Applicant's Arguments

- A) Applicant urges that Jahanshahi et al, Binder or Carruthers et al teach the selection of a subject with depression (such as major depression) or the selection of a subject with intermittent anxiety and depression.
- B) Applicant urges that Jahanshahi et al teach treatment of torticollis.
- C) Applicant urges that Binder does not teach, suggest or render obvious the treatment of major depression. Applicant urges that Binder does not teach, suggest or render obvious the introduction of botulinum toxin into a facial muscle that affects the ability of a subject to scowl or frown.

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- D) Carruthers et al teach cosmetic use of botulinum toxin.
- E) Applicant urges that one would not necessarily expect that the injection of botulinum toxin into a facial muscle would result in the alleviation of a major depression or alleviation of intermittent anxiety and depression.
- F) Applicant urges that a case of prima facie obviousness has not been established.
- G) Applicant refers to Exhibit A Finzi et al to point out unexpected results.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 26, 2006 have been fully considered but they are not persuasive.

- A) It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. It is the Examiner's position that the combination of references teaches the claimed invention. The combination of prior art references teach a method of treating depression and intermittent anxiety by administering botulinum toxin to a face muscle.

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B) To address Applicant comment's regarding Jahanshahi et al, while Jahanshahi et al teach patients that have toricollis, these patients also suffer from depression.

Jahanshahi et al teach that botulinum toxin reduced depression but there was no significant improvement in body concept and self-esteem (see the Abstract).

C) To address Applicant's arguments regarding Binder, Binder et al teach that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with emotional states such as depression and tension (column 1).

D) To address Applicant's arguments regarding Caruthers et al, Carruthers teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn mouth (see the Abstract).

E) To address Applicant comment regarding the combination of prior art references not teaching depression and intermittent anxiety, claims 1-7 and 16-18 are directed to methods of treating depression by administering botulinum toxin to facial muscles. As stated above, the combination of art references teach the claimed invention. It is the Examiner's position that the combination of references render the claimed invention obvious and based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to

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patients suffering from depression would be effective way to treat depression in these patients.

F) In response to applicant's argument that no case of *prima facie* obviousness was established the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case,

One of ordinary skill would be motivated to use botulinum toxin to administer botulinum toxin to patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Jahanshahi et al teach that administering botulinum toxin to torticollis patients experiencing depression significantly reduced levels of depression and anxiety, Binder teaches that botulinum toxin can be effectively administered to facial muscles such as the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth.

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G) To address Exhibit A, Finzi et al, while it is true that Finzi et al has established that botulinum toxin treats major depression, there is nothing on the record that suggest that the combination of references does not teach a method treating depression by administering to facial muscles of a patient botulinum toxin.

Claim 22 is directed to the method of claim 1, wherein the subject has major depression. Jahanshahi et al teach that 4 subjects used in the study were severely affected (e.g. major depressed according to the Beck Depression Inventory, (BDI))(page 230).

In view of all of the above, this rejection is maintained.

5. The rejection under 35 U.S.C. 103(a) is maintained for claims 1-7, 16-21 and newly submitted claim 22 for the reasons set forth on pages 6-8, paragraph 7 of the previous Office Action.

The rejection is reiterated below:

The rejection was on the grounds that the teaching of Jahanshahi et al, Binder and Carruthers et al have been described previously.

Jahanshahi et al, Binder and Carruthers et al do not teach an additional modality of treatment for depression.

Wagstaff et al teach that paroxetine is a selective serotonin reuptake inhibitor (SSRI) with antidepressant and anxiolytic activity (see the Abstract). Wagstaff et al teach that paroxetine is effective at treating depressive disorder (see the Abstract). Wagstaff et al teach that the common adverse effects with using paroxetine include headache (see the Abstract). Wagstaff et al teach that paroxetine is an important first-line option for treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, general anxiety disorder and post-traumatic stress disorder (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to use an additional modality of treatment for depression such as administration of SSRIs to

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patients suffering from depression because Jahanshahi et al suggest that use of other concepts may be helpful with direct management of psychological aspects such as body concept and low self-esteem. One of ordinary skill in the art would be motivated to administer SSRIs to treat patients with torticollis who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since Wagstaff et al teach that paroxetine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

Applicant's Arguments

- A) Applicant urges that Jahanshahi et al, Binder or Carruthers et al do not teach the selection of a subject with depression (such as major depression) or the selection of a subject with intermittent anxiety and depression.
- B) Applicant urges that Jahanshahi et al teach treatment of torticollis.
- C) Applicant urges that Binder does not teach, suggest or render obvious the treatment of major depression. Applicant urges that Binder does not teach, suggest or render obvious the introduction of botulinum toxin into a facial muscle that affects the ability of a subject to scowl or frown.
- D) Carruthers et al teach cosmetic used of botulinum toxin.
- E) Wagstaff et al teach the use of paroxetine.

- F) Applicant urges that a case of prima facie obviousness has not been established.
- G) Applicant urges that botulinum toxin is successful at treating patients when other treatments such as PAXIL or ZOLOFT have failed (Example 2 of the instant specification). Applicant urges that in view of unexpected results the combination of references do not make the claimed invention obvious.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 26, 2006 have been fully considered but they are not persuasive.

- A) It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. It is the Examiner's position that the combination of references teaches the claimed invention. The combination of prior art references teach a method of treating depression and intermittent anxiety by administering botulinum toxin to a face muscle.

B) To address Applicant comment's regarding Jahanshahi et al, while Jahanshahi et al teach patient that have toricollis, these patients also suffer from depression. Jahanshahi et al teach that botulinum toxin reduced depression but there was no significant improvement in body concept and self-esteem (see the Abstract).

C) To address Applicant's arguments regarding Binder, Binder et al teach that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with emotional states such as depression and tension (column 1).

D) To address Applicant's arguments regarding Caruthers et al, Carruthers teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn mouth (see the Abstract).

E) To address Applicant's arguments regarding Wagstaff et al, Wagstaff et al teach that paroxetine is a selective serotonin reuptake inhibitor (SSRI) with antidepressant and anxiolytic activity (see the Abstract). Wagstaff et al teach that paroxetine is effective at treating depressive disorder (see the Abstract). Wagstaff et al teach that the common adverse effects with using paroxetine include headache (see the Abstract). One of skill in the art would have been motivated to administer botulinum toxin to a patient suffering from depression because botulinum toxin is effective at treating depression as well as reducing the side effects of selective serotonin reuptake inhibitors such as headaches,

F) In response to applicant's argument that no case of *prima facie* obviousness was established the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case,

One of ordinary skill would be motivated to use botulinum toxin administer SSRIs to treat patients with torticollis who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of

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skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since Wagstaff et al teach that paroxetine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

G) To address Applicant's comments regarding unexpected superior results, as shown in (Example 2) of the instant specification there is nothing on the record that suggest that the combination of references does not teach a method treating depression by administering to facial muscles of a patient botulinum toxin and a selective serotonin reuptake inhibitor. It should be noted that the administration of botulinum toxin treats depression as well as the headaches that may be caused by administration of the serotonin reuptake inhibitor.

Claim 22 is directed to the method of claim 1, wherein the subject has major depression. Jahanshahi et al teach that 4 subjects used in the study had were severely affected (e.g. major depressed according to the Beck Depression Inventory, (BDI))(page 230).

In view of all of the above, this rejection is maintained.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Status of Claims

7. No claims allowed.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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